IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	Confirmation No.: 7147
PANDOL, *et al.*	Art Unit: 4173
Serial No.: 10/824,597	Examiner: Pagonakis, Anna
Filed: 15 April 2004	Atty. Dckt: 034044.021CIP1 (2002-428-2)
For: COMPOSITIONS COMPRISING PLANT-DERIVED POLYPHENOLIC COMPOUNDS AND INHIBITORS OF REACTIVE OXYGEN SPECIES AND METHODS OF USING THEREOF	

AFFIDAVIT OF DR. JINGZHEN YUAN

1. I, Jingzhen Yuan, reside at Culver City, CA.

2. I am employed by the University of California - Los Angeles as an Assistant Researcher.

3. A copy of my curriculum vitae is attached.

4. I have extensive knowledge of and research experience with pancreatic cancer and the Protein Kinase C (PKC) family of proteins.

5. I do not have any financial or other interest in the claimed invention.

6. In my opinion, one of ordinary skill in the art of PKC proteins, pancreatic cancer and pancreatitis would have at least a Ph.D. in biochemistry or molecular biology and/or an M.D. with research experience in biochemistry or molecular biology and diseases of the pancreas.

7. I am familiar with and understand the above-referenced patent application (Instant Application), the Response submitted herewith, and the claimed invention as set forth in the Response.

8. I am familiar with and understand the Office action mailed 13 November 2008 (Office action).

9. I am familiar with and understand the prior art cited on page 4 in the Office action. In particular, I have read and understand the following prior art references were cited by the Examiner:

   a. Schwartz (U.S. Patent 5,821,072)

   b. Gschwendt (1994) Biochem. Biophys. Res. Commun. 199(1):93-8

   c. Mouria (2002) Int. J. Cancer 98:761-769

10. It is my understanding that the Examiner's reasoning for rejecting the claimed invention as being obvious is as follows:

   a. Since Schwartz discloses that a PKC inhibitor can potentiate apoptosis in pancreatic

tumor cells if administered during or prior to an antitumor therapeutic agent and Gschwendt teaches that rottlerin is a PKC inhibitor, it would have been obvious to use rottlerin to treat pancreatic cancer with a reasonable likelihood of success; and

b. Further to the reasoning in paragraph 10a above, since Mouria discloses that genistein stimulates apoptosis and caspase activation in pancreatic cancer cells, it would have been obvious to administer rottlerin with genistein in order to treat pancreatic cancer in accordance with claims 38-40 of the claimed invention in the Instant Application.

11. In my opinion, the Examiner's reasoning for rejecting the claims is flawed as it is based on the implied (and incorrect) assertion that Schwartz teaches that all PKC inhibitors will be effective (e.g. induce apoptosis) against pancreatic cancer cells.

12. All PKC inhibitors are not effective against pancreatic cancer. In fact, experimental evidence in the art proves that all PKC inhibitors are not effective against in pancreatic cancer cells. For example, see:

a. Example 9A and Figures 29 and 30 of the Instant Application which shows that GF109203X (GF) and Ro-32-0432 (Ro), do not cause apoptosis (as evidenced by oligonucleosomal DNA fragmentation) in MIA PaCa-2 cells and PANC-1 cells, both of which are pancreatic cancer cell lines; and

b. Schwartz which states that: (a) "safingol alone did not induce significant levels of apoptosis" (col. 7, lines 35-37), and (b) RO 32-0432 alone had "essentially no effect on inducing apoptosis" (col. 18, lines 48-49). Safingol and RO 32-0432 are known PKC inhibitors.

13. It is my understanding that Schwartz actually teaches that the specific PKC inhibitors as tested do not induce apoptosis in cancer cells when administered without a chemotherapeutic agent. Thus, contrary to the Examiner's implied assertion, Schwartz does not teach or suggest that all PKC inhibitors will be effective against cancer cells.

14. Since all PKC inhibitors are not effective against cancer, and the specific PKC inhibitors tested by themselves, as taught by Schwartz, do not induce apoptosis in cancer cells, it is my opinion that one of ordinary skill in the art would not have been motivated to combine the teachings of Schwartz and Gschwendt in order to treat or inhibit pancreatic cancer or pancreatitis in a subject by administering rottlerin or a derivative thereof (i.e. a compound as set forth in claim 47) with a reasonable expectation of success.

15. It is my understanding that Schwartz and Mouria do not make any mention of rottlerin.

16. It is my understanding that Gschwendt does not make any mention of pancreatic cancer or pancreatitis.

17. Since Gschwendt does not mention anything about pancreatic cancer and pancreatitis and Schwartz does not teach that all PKC inhibitors will be effective against pancreatic cancer, it is my opinion that more than the fact that rottlerin is a PKC inhibitor is needed for one of ordinary skill in the art to have been motivated to treat or inhibit pancreatic cancer or pancreatitis in a subject by administering rottlerin or a derivative thereof (i.e. a compound as set forth in claim 47) with a reasonable expectation of success.

18. Since Mouria does not mention anything about rottlerin, it is my opinion that Mouria does not provide the requisite motivation (which is lacking in Schwartz and Gschwendt) in order for one of ordinary skill in the art to have been motivated to treat or inhibit pancreatic cancer or pancreatitis in a subject by administering rottlerin or a derivative thereof (i.e. a compound as set forth in claim 47) with a reasonable expectation of success.

19. It is my opinion that the disclosures of Schwartz, Gschwendt and Mouria, alone or in combination, do not provide the requisite teaching, suggestion or motivation for one of ordinary skill in the art to administer rottlerin or a derivative thereof (i.e. a compound as set forth in claim 47) to treat or inhibit pancreatic cancer or pancreatitis in a subject with a reasonable expectation of success.

20. In addition, as shown in the Instant Application, the ability of rottlerin to cause apoptosis is independent of any effects it may have on PKC. However, in my opinion, there is nothing in Schwartz, Gschwendt and Mouria, alone or in combination, to teach or suggest that rottlerin may cause apoptosis through a mechanism that is independent of any effects it may have on PKC such that one of ordinary skill in the art would administer rottlerin or a derivative thereof (i.e. a compound as set forth in claim 47) to treat or inhibit pancreatic cancer or pancreatitis in a subject with a reasonable expectation of success.

21. I hereby state that all statements made herein are of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patents issuing thereon.

Jingzhen Yuan

Dr. Jingzhen Yuan

Date: 04/10/09